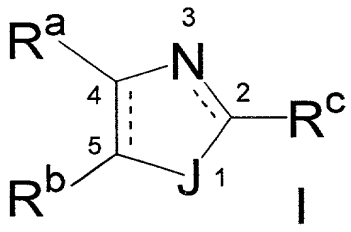
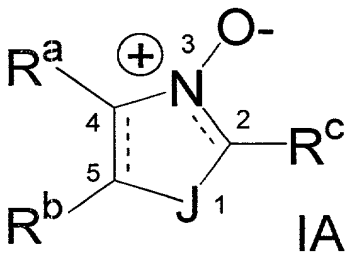
What is claimed:

1. A method of, in an animal, including a human, treating (i) diabetes or treating or ameliorating (ii) adverse sequelae of diabetes, (iii) kidney damage, (iv) damage to blood vasculature, atherosclerosis, peripheral vascular disease, coronary heart disease or heart failure, (v) hypertension, (vi) retinopathy, (vii) peripheral neuropathy, (viii) cataracts, (ix) osteoarthritis, (x) rheumatoid arthritis, (xi) Alzheimer's disease, (xii) damage to a tissue caused by contact with elevated levels of reducing sugars or (xiii) stroke, or (xiv) improving the elasticity or reducing wrinkles of the skin of an animal or (xv) increasing RBC deformability, comprising administering an effective amount of a compound of formula I or IA,



I

or



IA

wherein:

a. J is oxygen, sulfur, or N-R^d;

b. the carbon 2 to nitrogen bond is a double bond except when R^c is oxo;

c. the bond between carbons 4 and 5 is a single bond or a double bond;

d. R^a and R^b are

2. independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C1-C3)alkylenedioxy, allyl, amino, ω- alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), cycloalkyl, dialkylamino, halo, hydroxy, (C2-C6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, piperazin-1-yl, Ar {wherein, consistent with the rules of aromaticity, Ar is C_6 or C_{10} aryl or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N,

each heteroaryl ring can be fused to a substituted benzene, pyridine, pyrimidine, pyridazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Ar)}, Ar–alkyl, ArO-, $ArSO_2$-, ArSO-, ArS-, $ArSO_2NH$-, ArNH, (N-Ar)(N-alkyl)N-, ArC(O)-, ArC(O)NH-, ArNH-C(O)-, and (N-Ar)(N-alkyl)N-C(O)-, or together R_1 and R_2 comprise methylenedioxy-; or

2. together with their ring carbons form a C_6- or C_{10}- aryl fused ring; or

3. together with their ring carbons form a C_5-C_7 fused cycloalkyl ring having up to two double bonds including a fused double bond of the containing group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo; or

4. together with their ring carbons form a fused 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N; or

5. together with their ring carbons form a fused five to eight membered second heterocycle, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, sulfur, and $S(O)_n$, wherein n is 1 or 2;

b. R^d is alkyl, alkenyl, hydrogen, or Ar;

c. R^c is

1. oxo (when $\Delta^{2,3}$ is not present), or (when $\Delta^{2,3}$ is present) hydrogen, alkyl, alkylthio, hydrogen, mercapto, amino, amino(C_1-C_5)alkyl, amino(C_6 or C_{10})aryl, or wherein the amino of the last three groups can be substituted with

(a) Ar,

(b) Ar-Z-, Ar-alkyl-Z-, Ar-Z-alkyl, Ar-amino-Z-, Ar-aminoalkyl-Z-, or Ar-oxyalkyl-Z- , wherein Z is a carbonyl or -SO_2-

(c) formyl or alkanoyl, or

(d) up to two alkyl,

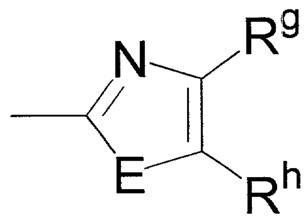
2. -$NHC(O)(CH_2)_n$-D-R^eR^f, wherein D is oxygen, sulfur or nitrogen, wherein where D is nitrogen n is 0,1 or 2, but when D is oxygen or sulfur n=1 or 2, and R^f is present only when D is nitrogen,

wherein

(a) R^e is

(1) Ar,

(2) a group of the formula



II

wherein E is sulfur, oxygen, or N-R^i , and R^g, R^h and R^i are independently the same as R^a, R^b and R^d, respectively,

(3) a C_3-C_8 cycloalkyl ring having up to one double bond with the proviso that the carbon linking the cyloalkyl ring to D is saturated, which cycloalkyl ring can be substituted by one or more alkyl-, alkoxycarbonyl-, amino-, aminocarbonyl-, carboxy-, fluoro-, or oxo-substituents;

(4) a 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of N for the 6-membered heteroaryl rings and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered heteroaryl rings;

(5) hydrogen, (C2-C6)hydroxyalkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkoxyimino), alkoxycarbonyl, a group Ar^{ϕ} which is C_6- or C_{10}- aryl or a 5- or 6-membered, or 9- or 10-membered heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar^{ϕ}–alkyl; and

(b) R^f is independently hydrogen, (C2-C6)hydroxyalkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, Ar^{ϕ}, or Ar^{ϕ}–alkyl;

wherein aryl, Ar, or Ar^{ϕ} can be substituted with, in addition to any substitutions specifically noted one or more substituents selected from the group of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C1-C3)alkylenedioxy, alkylsulfonyl,

alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, ArC(O)-, ArC(O)NH-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C2-C6)hydroxyalkyl, mercapto, nitro, ArO-, Ar-, Ar-alkyl-, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C6 or C10]arylpiperazin-1-yl-, 4-[C6 or C10]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperazin-1-yl, piperidin-1-yl; and

heterocycles, except those of Ar and Ar^{ϕ}, can be substituted with in addition to any substitutions specifically noted one or more substituents selected from acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C1 to C3)alkylenedioxy, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, ArC(O)-, ArO-, Ar-, Ar-alkyl, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, oxo, sulfamoyl, trifluoromethyl, 4-[C_6 or C_{10}]arylpiperidin-1-yl and 4-[C_6 or C_{10}]arylpiperazin-1-yl;

or a pharmaceutically acceptable salt of said compounds,

with the proviso that where the compound of formula I is administered to decrease intraocular pressure at least one compound of formula I administered in effective amount is not a thiazole substituted on a ring carbon sulfonamide (the amide of which can be substituted) that has carbonic anhydrase inhibiting activity.

2. The method of claim 1, comprising administering an effective amount of a compound of the formula I, wherein the bond between carbons 4 and 5 is a single bond.

3. The method of claim 1, comprising administering an effective amount of a compound of the formula I, wherein R^c is amino, amino(C_1-C_5)alkyl, or amino(C_6 or C_{10})aryl, or wherein the amino of any of the three groups can be substituted with

(a) Ar;

(b) Ar-Z-, Ar-alkyl-Z-, Ar-Z-alkyl, Ar-amino-Z-, Ar-aminoalkyl-Z-, or Ar-oxyalkyl-Z- , wherein Z is a carbonyl or -SO_2-; or

(c) formyl or alkanoyl.

4. The method of claim 1, comprising administering an effective amount of a compound of the formula I, wherein J is S or O, and R^c is hydrogen, oxo, alkyl, amino,

amino(C_1-C_5)alkyl or aminophenyl, wherein the amino of the latter three groups can be substituted with

(a) Ar;

(b) Ar-Z-, Ar-alkyl-Z-, Ar-Z-alkyl, Ar-amino-Z-, Ar-aminoalkyl-Z-, or Ar-oxyalkyl-Z- , wherein Z is a carbonyl or -SO_2-; or

(c) formyl or alkanoyl.

5. The method of Claim 1, comprising administering an effective amount of a compound of the formula I, wherein J is S, and R^c is hydrogen, oxo, alkyl, amino, amino(C_1-C_5)alkyl or aminophenyl, wherein the amino of the latter three groups can be substituted with

(a) Ar;

(b) Ar-Z-, Ar-alkyl-Z-, Ar-Z-alkyl, Ar-amino-Z-, Ar-aminoalkyl-Z-, or Ar-oxyalkyl-Z- , wherein Z is a carbonyl or -SO_2-; or

(c) formyl or alkanoyl.

6. The method of claim 1, comprising administering an effective amount of a compound of the formula I, wherein the compound is selected from the group consisting of thiazole, 2-amino-4-chlorobenzothiazole, 2,4,5-trimethylthiazole, 2-(3,5-dimethylphenoxy)-N-thiazol-2-yl)acetamide, 2-isobutylthiazole, (4-fluorophenyl)thiazolin-2-ylamine, 2-furyl-N-[4-(6-methylbenzothiazol-2-yl)phenyl]carboxamide, and 5,5-dimethyl-2-(2-naphthylamino)-4,5,6-trihydrobenzothiazol-7-one.

7. The method of claim 1, comprising administering an effective amount of a compound of the formula I, wherein

d. R^a and R^b are

1. independently selected from hydrogen, acylamino, alkanoyl, alkanoylalkyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, amino, ω-alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), cycloalkyl, dialkylamino, halo, hydroxy, (C2-C6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, morpholin-4-yl, thiomorpholin-4-yl,

piperidin-1-yl, piperazin-1-yl, Ar {wherein, consistent with the rules of aromaticity, Ar is C_6 or C_{10} aryl or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be fused to a substituted benzene, pyridine, pyrimidine, pyridazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Ar)}, Ar–alkyl, ArO-, $ArSO_2$-, ArSO-, ArS-, $ArSO_2NH$-, ArNH, (N-Ar)(N-alkyl)N-, ArC(O)-, ArC(O)NH-, ArNH-C(O)-, and (N-Ar)(N-alkyl)N-C(O)-; or

2. together with their ring carbons form a C_6- or C_{10}- aryl fused ring; or

3. together with their ring carbons form a C_5-C_7 fused cycloalkyl ring having no double bonds except a fused double bond of the formula I or IA ring, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, amino, aminocarbonyl, carboxy, fluoro, or oxo, where multiple substituents are located on different carbon atoms of the cycloalkyl ring, except in the case of alkyl and fluoro substituents, which can be located on the same or different carbon atoms; or

4. together with their ring carbons form a fused 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N; or

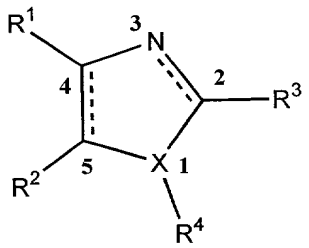
5. together with their ring carbons form a fused five to six membered second heterocycle, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, sulfur, and $S(O)_n$, wherein n is 1 or 2,

wherein aryl, Ar, or Ar^{ϕ} can be substituted with, in addition to any substitutions specifically noted one or more substituents selected from the group of alkyl, amino, dialkylamino, 1-pyrrolidinyl, 4-[C6 or C10]arylpiperazin-1-yl, 4-[C6 or C10]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperazin-1-yl, piperidin-1-yl; and

heterocycles, except those of Ar and Ar^{ϕ}, can be substituted with in addition to any substitutions specifically noted one or more substituents selected from acylamino,

alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C1 to C3)alkylenedioxy, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, ArC(O)-, ArO-, Ar-, Ar-alkyl, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, oxo, sulfamoyl, trifluoromethyl, 4-[C_6 or C_{10}]arylpiperidin-1-yl and 4-[C_6 or C_{10}]arylpiperazin-1-yl, wherein multiple substituents are located on different atoms of the heterocyclic ring, with the proviso that alkyl, alkoxycarbonyl, and fluoro substituents can be substituted on the same carbon atom of the heterocyclic ring.

8. A method of, in an animal, including a human, treating (i) diabetes or treating or ameliorating (ii) adverse sequelae of diabetes, (iii) kidney damage, (iv) damage to blood vasculature, atherosclerosis, peripheral vascular disease, coronary heart disease or heart failure, (v) hypertension, (vi) retinopathy, (vii) peripheral neuropathy, (viii) cataracts, (ix) osteoarthritis, (x) rheumatoid arthritis, (xi) Alzheimer's disease, (xii) damage to a tissue caused by contact with elevated levels of reducing sugars or (xiii) stroke, or (xiv) improving the elasticity or reducing wrinkles of the skin of an animal or (xv) increasing RBC deformability, comprising administering an effective amount of a compound of formula III:



III

wherein:

X is nitrogen or sulfur, provided that R^4 is present only when X is nitrogen;

the carbon 2 to nitrogen bond is a double bond except when R^3 is oxo;

the bond between carbons 4 and 5 is a single bond or a double bond;

R^1 and R^2

are independently hydrogen, hydroxyalkyl, (C2-C6)alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be

substituted with alkyloxyimino), alkoxycarbonyl, a group Ar which is (C_6-C_{10}) aryl or (C_5-C_9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl, or

together with their ring carbons form a C_6-C_{10} aromatic fused ring which can be substituted by one or more halo, amino, alkyl, sulfo, or sulfoalkyl, groups, or a C_1-C_3 alkylenedioxy group, with the proviso that when X is nitrogen R^1 and R^2 do not form a C_6 fused aromatic ring, or

together with their ring carbons form a C_5-C_7 fused cycloalkyl or cycloalkenyl ring having up to two double bonds including a fused double bond of the thiazole radical, which aliphatic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups;

R^4 is lower alkyl, lower alkenyl or Ar; and

R^3 is

(a) when X is S, R^3 is hydrogen, oxo, alkyl, amino, amino(C_1-C_5)alkyl or aminophenyl, wherein the amino of the latter three groups can be substituted with:

(i) Ar,

(ii) Ar-carbonyl, Ar-alkanoyl, Ar-carbonylalkyl, Ar-aminocarbonyl Ar-aminoalkanoyl or Ar-oxyalkanoyl or

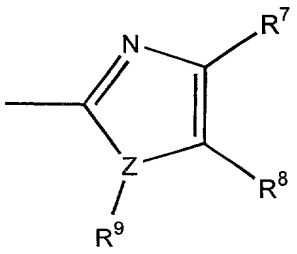
(iii) formyl or alkanoyl,

(b) $-NHC(O)(CH_2)_n-Y-R^5R^6$, wherein Y is oxygen, sulfur or nitrogen, n is 0 or 1, but n=1 when Y is oxygen or sulfur, and R^6 is present only when Y is nitrogen,

wherein R^5 is

(i) Ar,

(ii) a group of the formula



IV

wherein R^7, R^8 and R^9 are independently the same as R^1, R^2 and R^4, Z is sulfur or nitrogen, R^9 is present only when Z is nitrogen;

(iii) a C_3-C_8 cycloalkyl or cycloalkenyl ring having up to one double bond , which aliphatic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups;

(iv) a 3 to 8-membered heterocyclic ring wherein the heteroatom is one oxygen, one sulfur or one nitrogen, which heterocyclic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups,

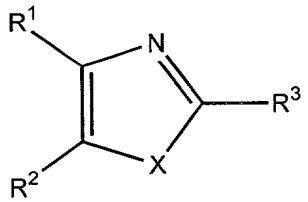
(iv) hydrogen, hydroxyalkyl, (C2-C6)alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, a group Ar which is (C_6-C_{10}) aryl or (C_5-C_9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl,

and R^6 is independently hydrogen, hydroxyalkyl, (C2-C6)alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, a group Ar which is (C6-C10) aryl or (C5-C9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl;

wherein each group Ar can be substituted by one or more halo, amino, alkyl, alkoxy, alkoxycarbonyl, sulfo, or sulfoalkyl, groups, or a C_1-C_3 alkylenedioxy group,

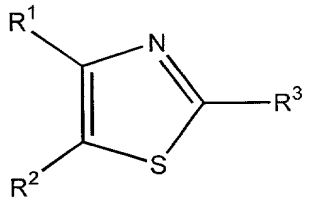
or a pharmaceutically acceptable salt of said compounds.

9. The method of claim 8, comprising administering an amount effective therefor of one or more compounds of the following formula:



V

10. The method of claim 8, comprising administering an amount effective therefor of one or more compounds of the following formula:

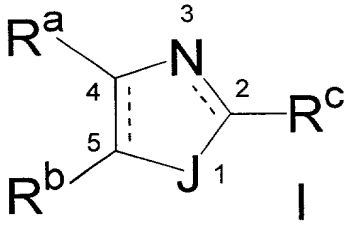


VI

wherein R^1, R^2 and R^3 are defined in claim 1.

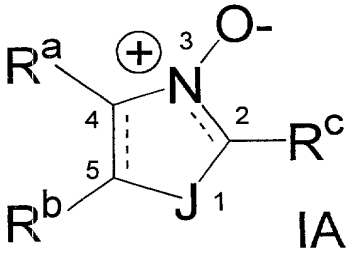
11. The method of claim 8, comprising administering an amount effective therefor of one or more compounds of formula **III**, wherein each Ar or cycloalkyl group is substituted with up to two substituents.

12. A method of, in an animal, including a human, reducing tissue damage caused by dialysis, comprising, in peritoneal dialysis, administering with a dialysis composition an effective amount of a compound of formula I or IA, or, in hemodialysis, providing in an exchange fluid an effective amount of a compound of formula I or IA, wherein compounds of formula I or IA are as follows:



I

or



IA

wherein:

a. J is oxygen, sulfur, or N-R^d;

b. the carbon 2 to nitrogen bond is a double bond except when R^c is oxo;

c. the bond between carbons 4 and 5 is a single bond or a double bond;

d. R^a and R^b are

3. independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C1-C3)alkylenedioxy, allyl, amino, ω- alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), cycloalkyl, dialkylamino, halo, hydroxy, (C2-C6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, piperazin-1-yl, Ar {wherein, consistent with the rules of aromaticity, Ar is C_6 or C_{10} aryl or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be fused to a substituted benzene, pyridine, pyrimidine, pyridazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Ar)}, Ar–alkyl, ArO-, $ArSO_2$-, ArSO-, ArS-, $ArSO_2NH$-, ArNH, (N-Ar)(N-alkyl)N-, ArC(O)-, ArC(O)NH-, ArNH-C(O)-, and (N-Ar)(N-alkyl)N-C(O)-, or together R_1 and R_2 comprise methylenedioxy-; or

2. together with their ring carbons form a C_6- or C_{10}- aryl fused ring; or

3. together with their ring carbons form a C_5-C_7 fused cycloalkyl ring having up to two double bonds including a fused double bond of the containing group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo; or

4. together with their ring carbons form a fused 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N; or

5. together with their ring carbons form a fused five to eight membered second heterocycle, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, sulfur, and $S(O)_n$, wherein n is 1 or 2;

b. R^d is alkyl, alkenyl, hydrogen, or Ar;

c. R^c is

1. oxo (when $\Delta^{2,3}$ is not present), or (when $\Delta^{2,3}$ is present) hydrogen, alkyl, alkylthio, hydrogen, mercapto, amino, amino(C_1-C_5)alkyl, amino(C_6 or C_{10})aryl, or wherein the amino of the last three groups can be substituted with

(a) Ar,

(b) Ar-Z-, Ar-alkyl-Z-, Ar-Z-alkyl, Ar-amino-Z-, Ar-aminoalkyl-Z-, or Ar-oxyalkyl-Z- , wherein Z is a carbonyl or -SO_2-

(c) formyl or alkanoyl,, or

(d) up to two alkyl,

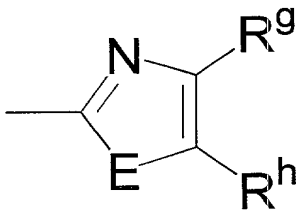
2. -$NHC(O)(CH_2)_n$-D-R^eR^f, wherein D is oxygen, sulfur or nitrogen, wherein where D is nitrogen n is 0,1 or 2, but when D is oxygen or sulfur n=1 or 2, and R^f is present only when D is nitrogen,

wherein

(a) R^e is

(1) Ar,

(2) a group of the formula



II

wherein E is sulfur, oxygen, or N-R^i , and R^g, R^h and R^i are independently the same as R^a, R^b and R^d, respectively,

(3) a C_3-C_8 cycloalkyl ring having up to one double bond with the proviso that the carbon linking the cyloalkyl ring to D is saturated, which cycloalkyl ring can be substituted by one or more alkyl-, alkoxycarbonyl-, amino-, aminocarbonyl-, carboxy-, fluoro-, or oxo-substituents;

(4) a 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of N for the 6-membered heteroaryl rings and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered heteroaryl rings;

(5) hydrogen, (C2-C6)hydroxyalkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkoxyimino), alkoxycarbonyl, a group Ar^{ϕ} which is C_6- or C_{10}- aryl or a 5- or 6-membered, or 9- or 10-membered heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar^{ϕ}–alkyl; and

(b) R^f is independently hydrogen, (C2-C6)hydroxyalkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, Ar^{ϕ}, or Ar^{ϕ}–alkyl;

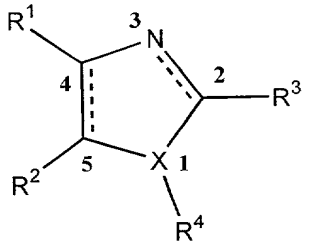
wherein aryl, Ar, or Ar^{ϕ} can be substituted with, in addition to any substitutions specifically noted one or more substituents selected from the group of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C1-C3)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, ArC(O)-, ArC(O)NH-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C2-C6)hydroxyalkyl, mercapto, nitro, ArO-, Ar-, Ar-alkyl-, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C6 or C10]arylpiperazin-1-yl-, 4-[C6 or C10]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperazin-1-yl, piperidin-1-yl; and

heterocycles, except those of Ar and Ar^{ϕ}, can be substituted with in addition to any substitutions specifically noted one or more substituents selected from acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C1 to C3)alkylenedioxy, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, ArC(O)-, ArO-, Ar-, Ar-alkyl, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, oxo, sulfamoyl, trifluoromethyl, 4-[C_6 or C_{10}]arylpiperidin-1-yl and 4-[C_6 or C_{10}]arylpiperazin-1-yl;

or a pharmaceutically acceptable salt of said compounds,

with the proviso that where the compound of formula I is administered to decrease intraocular pressure at least one compound of formula I administered in effective amount is not a thiazole substituted on a ring carbon sulfonamide (the amide of which can be substituted) that has carbonic anhydrase inhibiting activity.

13. A method of, in an animal, including a human, reducing tissue damage caused by dialysis, comprising, in peritoneal dialysis, administering with a dialysis composition an effective amount of a compound of formula III, or, in hemodialysis, providing in an exchange fluid an effective amount of a compound of formula III, wherein compounds of formula III are as follows:



III

wherein:

X is nitrogen or sulfur, provided that R^4 is present only when X is nitrogen;

the carbon 2 to nitrogen bond is a double bond except when R^3 is oxo;

the bond between carbons 4 and 5 is a single bond or a double bond;

R^1 and R^2

are independently hydrogen, hydroxyalkyl, (C2-C6)alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, a group Ar which is (C_6-C_{10}) aryl or (C_5-C_9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl, or

together with their ring carbons form a C_6-C_{10} aromatic fused ring which can be substituted by one or more halo, amino, alkyl, sulfo, or sulfoalkyl, groups, or a C_1-C_3 alkylenedioxy group, with the proviso that when X is nitrogen R^1 and R^2 do not form a C_6 fused aromatic ring, or

together with their ring carbons form a C_5-C_7 fused cycloalkyl or cycloalkenyl ring having up to two double bonds including a fused double bond of the thiazole radical, which aliphatic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups;

R^4 is lower alkyl, lower alkenyl or Ar; and

R^3 is

(a) when X is S, R^3 is hydrogen, oxo, alkyl, amino, amino(C_1-C_5)alkyl or aminophenyl, wherein the amino of the latter three groups can be substituted with:

(i) Ar,

(ii) Ar-carbonyl, Ar-alkanoyl, Ar-carbonylalkyl, Ar-aminocarbonyl Ar-aminoalkanoyl or Ar-oxyalkanoyl or

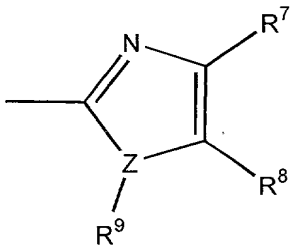
(iii) formyl or alkanoyl,

(b) -NHC(O)$(CH_2)_n$-Y-R^5R^6, wherein Y is oxygen, sulfur or nitrogen, n is 0 or 1, but n=1 when Y is oxygen or sulfur, and R^6 is present only when Y is nitrogen,

wherein R^5 is

(i) Ar,

(ii) a group of the formula



IV

wherein R^7, R^8 and R^9 are independently the same as R^1, R^2 and R^4, Z is sulfur or nitrogen, R^9 is present only when Z is nitrogen;

(iii) a C_3-C_8 cycloalkyl or cycloalkenyl ring having up to one double bond , which aliphatic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups;

(iv) a 3 to 8-membered heterocyclic ring wherein the heteroatom is one oxygen, one sulfur or one nitrogen, which heterocyclic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups,

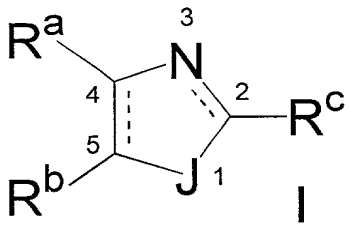
(iv) hydrogen, hydroxyalkyl, (C2-C6)alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, a group Ar

which is (C_6-C_{10}) aryl or (C_5-C_9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl,

and R^6 is independently hydrogen, hydroxyalkyl, (C2-C6)alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, a group Ar which is (C6-C10) aryl or (C5-C9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl;

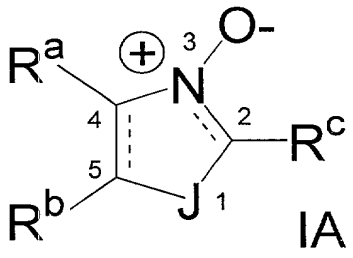
wherein each group Ar can be substituted by one or more halo, amino, alkyl, alkoxy, alkoxycarbonyl, sulfo, or sulfoalkyl, groups, or a C_1-C_3 alkylenedioxy group, or a pharmaceutically acceptable salt of said compounds.

14. A method of, in an animal, including a human, decreasing or ameliorating bone loss comprising administering an effective amount of a compound of formula I or IA:



I

or



IA

wherein:

a. J is oxygen, sulfur, or N-R^d;

b. the carbon 2 to nitrogen bond is a double bond except when R^c is oxo;

c. the bond between carbons 4 and 5 is a single bond or a double bond;

d. R^a and R^b are

4. independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C1-C3)alkylenedioxy, allyl, amino, ω- alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), cycloalkyl, dialkylamino, halo, hydroxy, (C2-C6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio,

trifluoromethyl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, piperazin-1-yl, Ar {wherein, consistent with the rules of aromaticity, Ar is C_6 or C_{10} aryl or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be fused to a substituted benzene, pyridine, pyrimidine, pyridazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Ar)}, Ar–alkyl, ArO-, $ArSO_2$-, ArSO-, ArS-, $ArSO_2NH$-, ArNH, (N-Ar)(N-alkyl)N-, ArC(O)-, ArC(O)NH-, ArNH-C(O)-, and (N-Ar)(N-alkyl)N-C(O)-, or together R_1 and R_2 comprise methylenedioxy-; or

2. together with their ring carbons form a C_6- or C_{10}- aryl fused ring; or

3. together with their ring carbons form a C_5-C_7 fused cycloalkyl ring having up to two double bonds including a fused double bond of the containing group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo; or

4. together with their ring carbons form a fused 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N; or

5. together with their ring carbons form a fused five to eight membered second heterocycle, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, sulfur, and $S(O)_n$, wherein n is 1 or 2;

b. R^d is alkyl, alkenyl, hydrogen, or Ar;

c. R^c is

1. oxo (when $\Delta^{2,3}$ is not present), or (when $\Delta^{2,3}$ is present) hydrogen, alkyl, alkylthio, hydrogen, mercapto, amino, amino(C_1-C_5)alkyl, amino(C_6 or C_{10})aryl, or wherein the amino of the last three groups can be substituted with

(a) Ar,

(b) Ar-Z-, Ar-alkyl-Z-, Ar-Z-alkyl, Ar-amino-Z-, Ar-aminoalkyl-Z-, or Ar-oxyalkyl-Z- , wherein Z is a carbonyl or $-SO_2-$

(c) formyl or alkanoyl, or

(d) up to two alkyl,

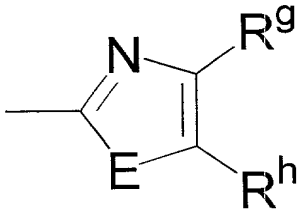
2. -NHC(O)$(CH_2)_n$-D-R^eR^f, wherein D is oxygen, sulfur or nitrogen, wherein where D is nitrogen n is 0,1 or 2, but when D is oxygen or sulfur n=1 or 2, and R^f is present only when D is nitrogen,

wherein

(a) R^e is

(1) Ar,

(2) a group of the formula



II

wherein E is sulfur, oxygen, or N-R^i , and R^g, R^h and R^i are independently the same as R^a, R^b and R^d, respectively,

(3) a C_3-C_8 cycloalkyl ring having up to one double bond with the proviso that the carbon linking the cyloalkyl ring to D is saturated, which cycloalkyl ring can be substituted by one or more alkyl-, alkoxycarbonyl-, amino-, aminocarbonyl-, carboxy-, fluoro-, or oxo-substituents;

(4) a 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of N for the 6-membered heteroaryl rings and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered heteroaryl rings;

(5) hydrogen, (C2-C6)hydroxyalkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkoxyimino), alkoxycarbonyl, a group Ar^ϕ which is C_6- or C_{10}- aryl or a 5- or 6-membered, or 9- or 10-membered heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar^ϕ–alkyl; and

(b) R^f is independently hydrogen, (C2-C6)hydroxyalkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, Ar^{ϕ}, or Ar^{ϕ}–alkyl;

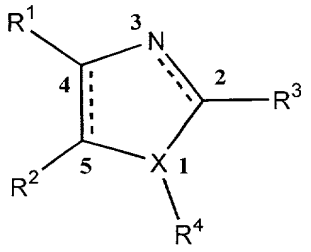
wherein aryl, Ar, or Ar^{ϕ} can be substituted with, in addition to any substitutions specifically noted one or more substituents selected from the group of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C1-C3)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, ArC(O)-, ArC(O)NH-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C2-C6)hydroxyalkyl, mercapto, nitro, ArO-, Ar-, Ar-alkyl-, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C6 or C10]arylpiperazin-1-yl-, 4-[C6 or C10]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperazin-1-yl, piperidin-1-yl; and

heterocycles, except those of Ar and Ar^{ϕ}, can be substituted with in addition to any substitutions specifically noted one or more substituents selected from acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C1 to C3)alkylenedioxy, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, ArC(O)-, ArO-, Ar-, Ar-alkyl, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, oxo, sulfamoyl, trifluoromethyl, 4-[C_6 or C_{10}]arylpiperidin-1-yl and 4-[C_6 or C_{10}]arylpiperazin-1-yl;

or a pharmaceutically acceptable salt of said compounds,

with the proviso that where the compound of formula I is administered to decrease intraocular pressure at least one compound of formula I administered in effective amount is not a thiazole substituted on a ring carbon sulfonamide (the amide of which can be substituted) that has carbonic anhydrase inhibiting activity.

15. A method of, in an animal, including a human, decreasing or ameliorating bone loss comprising administering an effective amount of a compound of formula III:



III

wherein:

X is nitrogen or sulfur, provided that R^4 is present only when X is nitrogen;

the carbon 2 to nitrogen bond is a double bond except when R^3 is oxo;

the bond between carbons 4 and 5 is a single bond or a double bond;

R^1 and R^2

are independently hydrogen, hydroxyalkyl, (C2-C6)alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, a group Ar which is (C_6-C_{10}) aryl or (C_5-C_9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl, or

together with their ring carbons form a C_6-C_{10} aromatic fused ring which can be substituted by one or more halo, amino, alkyl, sulfo, or sulfoalkyl, groups, or a C_1-C_3 alkylenedioxy group, with the proviso that when X is nitrogen R^1 and R^2 do not form a C_6 fused aromatic ring, or

together with their ring carbons form a C_5-C_7 fused cycloalkyl or cycloalkenyl ring having up to two double bonds including a fused double bond of the thiazole radical, which aliphatic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups;

R^4 is lower alkyl, lower alkenyl or Ar; and

R^3 is

(a) when X is S, R^3 is hydrogen, oxo, alkyl, amino, amino(C_1-C_5)alkyl or aminophenyl, wherein the amino of the latter three groups can be substituted with:

(i) Ar,

(ii) Ar-carbonyl, Ar-alkanoyl, Ar-carbonylalkyl, Ar-aminocarbonyl Ar-aminoalkanoyl or Ar-oxyalkanoyl or

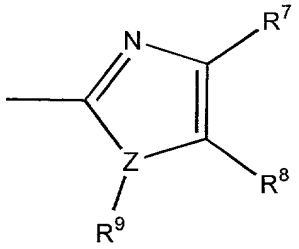
(iii) formyl or alkanoyl,

(b) $-NHC(O)(CH_2)_n-Y-R^5R^6$, wherein Y is oxygen, sulfur or nitrogen, n is 0 or 1, but n=1 when Y is oxygen or sulfur, and R^6 is present only when Y is nitrogen,

wherein R^5 is

(i) Ar,

(ii) a group of the formula



IV

wherein R^7, R^8 and R^9 are independently the same as R^1, R^2 and R^4, Z is sulfur or nitrogen, R^9 is present only when Z is nitrogen;

(iii) a C_3-C_8 cycloalkyl or cycloalkenyl ring having up to one double bond , which aliphatic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups;

(iv) a 3 to 8-membered heterocyclic ring wherein the heteroatom is one oxygen, one sulfur or one nitrogen, which heterocyclic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups,

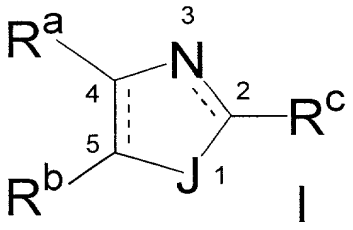
(iv) hydrogen, hydroxyalkyl, (C2-C6)alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, a group Ar which is (C_6-C_{10}) aryl or (C_5-C_9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl,

and R^6 is independently hydrogen, hydroxyalkyl, (C2-C6)alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be

substituted with alkyloxyimino), alkoxycarbonyl, a group Ar which is (C6-C10) aryl or (C5-C9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl;

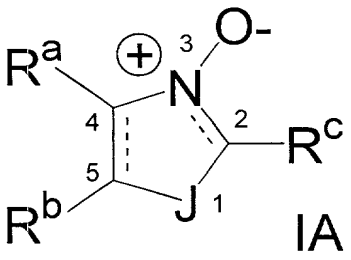
wherein each group Ar can be substituted by one or more halo, amino, alkyl, alkoxy, alkoxycarbonyl, sulfo, or sulfoalkyl, groups, or a C_1-C_3 alkylenedioxy group, or a pharmaceutically acceptable salt of said compounds.

16. A method of, in an animal, including a human, treating or ameliorating sickle cell disease comprising administering an effective amount of a compound of formula I or IA:



I

or



IA

wherein:

a. J is oxygen, sulfur, or N-R^d;

b. the carbon 2 to nitrogen bond is a double bond except when R^c is oxo;

c. the bond between carbons 4 and 5 is a single bond or a double bond;

d. R^a and R^b are

5. independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C1-C3)alkylenedioxy, allyl, amino, ω- alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), cycloalkyl, dialkylamino, halo, hydroxy, (C2-C6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, piperazin-1-yl, Ar {wherein, consistent with the rules of aromaticity, Ar is C_6 or C_{10} aryl or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N,

each heteroaryl ring can be fused to a substituted benzene, pyridine, pyrimidine, pyridazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Ar)}, Ar–alkyl, ArO-, $ArSO_2$-, ArSO-, ArS-, $ArSO_2NH$-, ArNH, (N-Ar)(N-alkyl)N-, ArC(O)-, ArC(O)NH-, ArNH-C(O)-, and (N-Ar)(N-alkyl)N-C(O)-, or together R_1 and R_2 comprise methylenedioxy-; or

2. together with their ring carbons form a C_6- or C_{10}- aryl fused ring; or

3. together with their ring carbons form a C_5-C_7 fused cycloalkyl ring having up to two double bonds including a fused double bond of the containing group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo; or

4. together with their ring carbons form a fused 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N; or

5. together with their ring carbons form a fused five to eight membered second heterocycle, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, sulfur, and $S(O)_n$, wherein n is 1 or 2;

b. R^d is alkyl, alkenyl, hydrogen, or Ar;

c. R^c is

1. oxo (when $\Delta^{2,3}$ is not present), or (when $\Delta^{2,3}$ is present) hydrogen, alkyl, alkylthio, hydrogen, mercapto, amino, amino(C_1-C_5)alkyl, amino(C_6 or C_{10})aryl, or wherein the amino of the last three groups can be substituted with

(a) Ar,

(b) Ar-Z-, Ar-alkyl-Z-, Ar-Z-alkyl, Ar-amino-Z-, Ar-aminoalkyl-Z-, or Ar-oxyalkyl-Z- , wherein Z is a carbonyl or -SO_2-

(c) formyl or alkanoyl, or

(d) up to two alkyl,

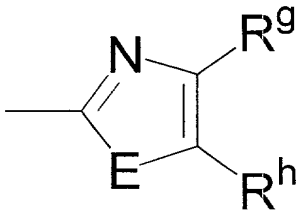
2. -$NHC(O)(CH_2)_n$-D-R^eR^f, wherein D is oxygen, sulfur or nitrogen, wherein where D is nitrogen n is 0,1 or 2, but when D is oxygen or sulfur n=1 or 2, and R^f is present only when D is nitrogen,

wherein

(a) R^e is

(1) Ar,

(2) a group of the formula



II

wherein E is sulfur, oxygen, or N-R^i , and R^g, R^h and R^i are independently the same as R^a, R^b and R^d, respectively,

(3) a C_3-C_8 cycloalkyl ring having up to one double bond with the proviso that the carbon linking the cyloalkyl ring to D is saturated, which cycloalkyl ring can be substituted by one or more alkyl-, alkoxycarbonyl-, amino-, aminocarbonyl-, carboxy-, fluoro-, or oxo-substituents;

(4) a 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of N for the 6-membered heteroaryl rings and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered heteroaryl rings;

(5) hydrogen, (C2-C6)hydroxyalkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkoxyimino), alkoxycarbonyl, a group Ar^ϕ which is C_6- or C_{10}- aryl or a 5- or 6-membered, or 9- or 10-membered heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar^ϕ–alkyl; and

(b) R^f is independently hydrogen, (C2-C6)hydroxyalkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, Ar^ϕ, or Ar^ϕ–alkyl;

wherein aryl, Ar, or Ar^ϕ can be substituted with, in addition to any substitutions specifically noted one or more substituents selected from the group of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C1-C3)alkylenedioxy, alkylsulfonyl,

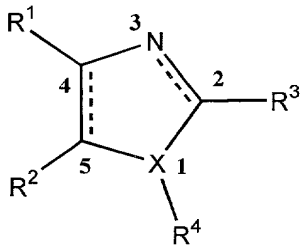
alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, ArC(O)-, ArC(O)NH-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C2-C6)hydroxyalkyl, mercapto, nitro, ArO-, Ar-, Ar-alkyl-, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C6 or C10]arylpiperazin-1-yl-, 4-[C6 or C10]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperazin-1-yl, piperidin-1-yl; and

heterocycles, except those of Ar and Ar^{ϕ}, can be substituted with in addition to any substitutions specifically noted one or more substituents selected from acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C1 to C3)alkylenedioxy, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, ArC(O)-, ArO-, Ar-, Ar-alkyl, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, oxo, sulfamoyl, trifluoromethyl, 4-[C_6 or C_{10}]arylpiperidin-1-yl and 4-[C_6 or C_{10}]arylpiperazin-1-yl;

or a pharmaceutically acceptable salt of said compounds,

with the proviso that where the compound of formula I is administered to decrease intraocular pressure at least one compound of formula I administered in effective amount is not a thiazole substituted on a ring carbon sulfonamide (the amide of which can be substituted) that has carbonic anhydrase inhibiting activity.

17. A method of, in an animal, including a human, treating or ameliorating sickle cell disease comprising administering an effective amount of a compound of formula III:



III

wherein:

X is nitrogen or sulfur, provided that R^4 is present only when X is nitrogen;

the carbon 2 to nitrogen bond is a double bond except when R^3 is oxo;

the bond between carbons 4 and 5 is a single bond or a double bond;

R^1 and R^2

are independently hydrogen, hydroxyalkyl, (C2-C6)alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, a group Ar which is (C_6-C_{10}) aryl or (C_5-C_9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl, or

together with their ring carbons form a C_6-C_{10} aromatic fused ring which can be substituted by one or more halo, amino, alkyl, sulfo, or sulfoalkyl, groups, or a C_1-C_3 alkylenedioxy group, with the proviso that when X is nitrogen R^1 and R^2 do not form a C_6 fused aromatic ring, or

together with their ring carbons form a C_5-C_7 fused cycloalkyl or cycloalkenyl ring having up to two double bonds including a fused double bond of the thiazole radical, which aliphatic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups;

R^4 is lower alkyl, lower alkenyl or Ar; and

R^3 is

(a) when X is S, R^3 is hydrogen, oxo, alkyl, amino, amino(C_1-C_5)alkyl or aminophenyl, wherein the amino of the latter three groups can be substituted with:

(i) Ar,

(ii) Ar-carbonyl, Ar-alkanoyl, Ar-carbonylalkyl, Ar-aminocarbonyl Ar-aminoalkanoyl or Ar-oxyalkanoyl or

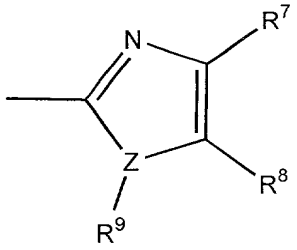
(iii) formyl or alkanoyl,

(b) -NHC(O)$(CH_2)_n$-Y-R^5R^6, wherein Y is oxygen, sulfur or nitrogen, n is 0 or 1, but n=1 when Y is oxygen or sulfur, and R^6 is present only when Y is nitrogen,

wherein R^5 is

(i) Ar,

(ii) a group of the formula



IV

wherein R^7, R^8 and R^9 are independently the same as R^1, R^2 and R^4, Z is sulfur or nitrogen, R^9 is present only when Z is nitrogen;

(iii) a C_3-C_8 cycloalkyl or cycloalkenyl ring having up to one double bond , which aliphatic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups;

(iv) a 3 to 8-membered heterocyclic ring wherein the heteroatom is one oxygen, one sulfur or one nitrogen, which heterocyclic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups,

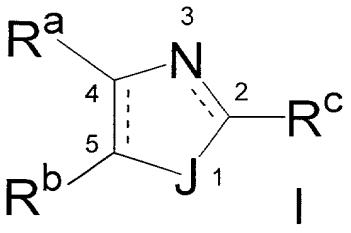
(iv) hydrogen, hydroxyalkyl, (C2-C6)alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, a group Ar which is (C_6-C_{10}) aryl or (C_5-C_9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl,

and R^6 is independently hydrogen, hydroxyalkyl, (C2-C6)alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, a group Ar which is (C6-C10) aryl or (C5-C9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl;

wherein each group Ar can be substituted by one or more halo, amino, alkyl, alkoxy, alkoxycarbonyl, sulfo, or sulfoalkyl, groups, or a C_1-C_3 alkylenedioxy group,

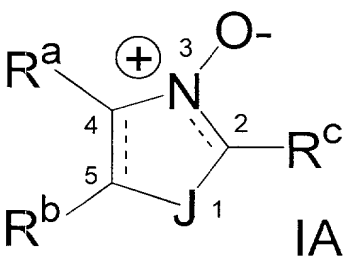
or a pharmaceutically acceptable salt of said compounds.

18. A compound of formula I or IA,



I

or



IA

wherein:

a. J is oxygen, sulfur, or N-R^d;

b. the carbon 2 to nitrogen bond is a double bond except when R^c is oxo;

c. the bond between carbons 4 and 5 is a single bond or a double bond;

d. R^a and R^b are

6. independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C1-C3)alkylenedioxy, allyl, amino, ω- alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), cycloalkyl, dialkylamino, halo, hydroxy, (C2-C6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, piperazin-1-yl, Ar {wherein, consistent with the rules of aromaticity, Ar is C_6 or C_{10} aryl or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be fused to a substituted benzene, pyridine, pyrimidine, pyridazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Ar)}, Ar–alkyl, ArO-, $ArSO_2$-, ArSO-, ArS-, $ArSO_2NH$-, ArNH, (N-Ar)(N-alkyl)N-, ArC(O)-, ArC(O)NH-, ArNH-C(O)-, and (N-Ar)(N-alkyl)N-C(O)-, or together R_1 and R_2 comprise methylenedioxy-, wherein at least one of R^a and R^b is other than hydrogen; or

2. together with their ring carbons form a C_6- or C_{10}- aryl fused ring; or

3. together with their ring carbons form a C_5-C_7 fused cycloalkyl ring having up to two double bonds including a fused double bond of the containing group, which

cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo; or

4. together with their ring carbons form a fused 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N; or

5. together with their ring carbons form a fused five to eight membered second heterocycle, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, sulfur, and $S(O)_n$, wherein n is 1 or 2;

b. R^d is alkyl, alkenyl, hydrogen, or Ar;

c. R^c is

1. dialkylamino(C_1-C_5)alkyl; or

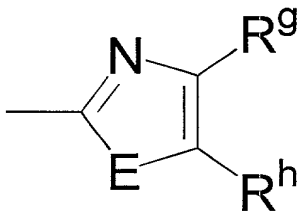
2. -$NHC(O)(CH_2)_n$-D-R^eR^f, wherein D is oxygen, sulfur or nitrogen, wherein where D is nitrogen n is 0,1 or 2, but when D is oxygen or sulfur n=1 or 2, and R^f is present only when D is nitrogen,

wherein

(a) R^e is

(1) Ar,

(2) a group of the formula



II

wherein E is sulfur, oxygen, or N-R^i, and R^g, R^h and R^i are independently the same as R^a, R^b and R^d, respectively,

(3) a C_3-C_8 cycloalkyl ring having up to one double bond with the proviso that the carbon linking the cyloalkyl ring to D is saturated, which cycloalkyl ring can be substituted by one or more alkyl-, alkoxycarbonyl-, amino-, aminocarbonyl-, carboxy-, fluoro-, or oxo-substituents; or

(4) a 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of N for the 6-membered heteroaryl rings and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered heteroaryl rings; or

(5) hydrogen, (C2-C6)hydroxyalkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkoxyimino), alkoxycarbonyl, a group Ar^{ϕ} which is C_6- or C_{10}- aryl or a 5- or 6-membered, or 9- or 10-membered heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar^{ϕ}–alkyl; and

(b) R^f is independently hydrogen, (C2-C6)hydroxyalkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, Ar^{ϕ}, or Ar^{ϕ}–alkyl;

wherein aryl, Ar, or Ar^{ϕ} can be substituted with, in addition to any substitutions specifically noted one or more substituents selected from the group of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C1-C3)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, ArC(O)-, ArC(O)NH-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C2-C6)hydroxyalkyl, mercapto, nitro, ArO-, Ar-, Ar-alkyl-, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C6 or C10]arylpiperazin-1-yl-, 4-[C6 or C10]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperazin-1-yl, piperidin-1-yl; and

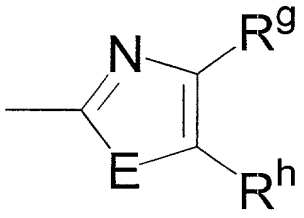
heterocycles, except those of Ar and Ar^{ϕ}, can be substituted with in addition to any substitutions specifically noted one or more substituents selected from acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C1 to C3)alkylenedioxy, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, ArC(O)-, ArO-, Ar-, Ar-alkyl, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, oxo, sulfamoyl, trifluoromethyl, 4-[C_6 or C_{10}]arylpiperidin-1-yl and 4-[C_6 or C_{10}]arylpiperazin-1-yl.

19. The compound of claim 18, wherein D is oxygen or sulfur.

20. The compound of claim 19, wherein R^e is

(1) Ar,

(2) a group of the formula



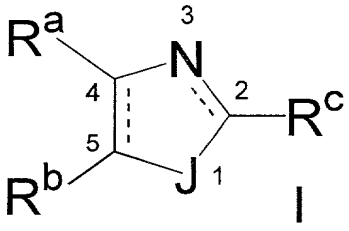
II

wherein E is sulfur, oxygen, or N-R^i, and R^g, R^h and R^i are independently the same as R^a, R^b and R^d, respectively,

(3) a C_3-C_8 cycloalkyl ring having up to one double bond with the proviso that the carbon linking the cyloalkyl ring to D is saturated, which cycloalkyl ring can be substituted by one or more alkyl-, alkoxycarbonyl-, amino-, aminocarbonyl-, carboxy-, fluoro-, or oxo-substituents; or

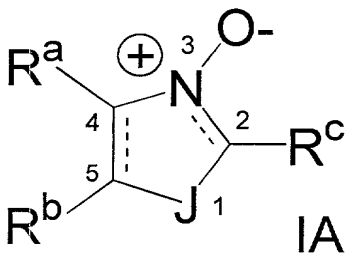
(4) a 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of N for the 6-membered heteroaryl rings and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered heteroaryl rings.

21. A compound of formula I or IA,



I

or



IA

wherein:

a. J is sulfur;

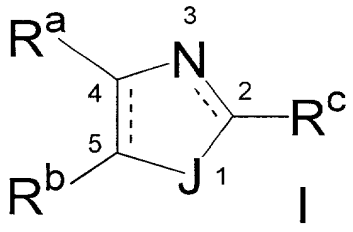
b. R^a is hydroxyalkyl or alkyl omega-substituted with a tertiary amine which is dialkyl amine or (i) incorporated into a 5- or 6-membered heteroaryl ring, wherein the 6-

membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and one to two atoms of N or (ii) incorporated into a 5- or 6-membered non-aromatic heterocyclic ring having one to two ring nitrogens; and

c. R^b and R^c are alkyl.

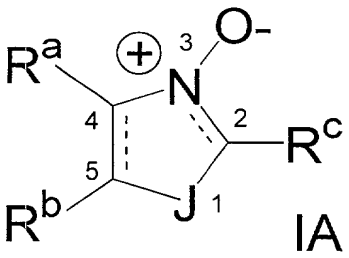
22. A method of treating an indication of the invention comprising administering an effective amount of a compound of claim 21.

23. A compound of formula I or IA,



I

or



IA

wherein:

a. J is sulfur;

b. the carbon 2 to nitrogen bond is a double bond;

c. the bond between carbons 4 and 5 is a double bond;

d. R^a and R^b are independently selected from hydrogen, acylamino, alkanoyl, alkanoylalkyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C2-C6)hydroxyalkyl, nitro, trifluoromethyl, Ar **{**wherein, Ar is C_6 or C_{10} aryl**}**, or Ar–alkyl; and

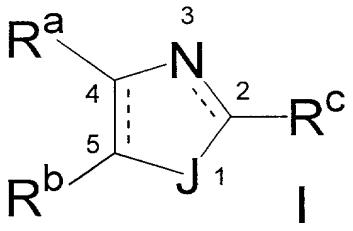
c. R^c is alkyl omega-substituted with a tertiary amine which is dialkyl amine or (i) incorporated into a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and one to two atoms of N or (ii) incorporated into a 5- or 6-membered non-aromatic heterocyclic ring having one to two ring nitrogens,

wherein aryl can be substituted with one or more substituents selected from the group of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy,

alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C1-C3)alkylenedioxy, alkylthio, allyl, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C2-C6)hydroxyalkyl, mercapto, nitro, ArO-, Ar-, or Ar-alkyl-.

24. A method of treating an indication of the invention comprising administering an effective amount of a compound of claim 23.

25. A compound of formula I or IA,



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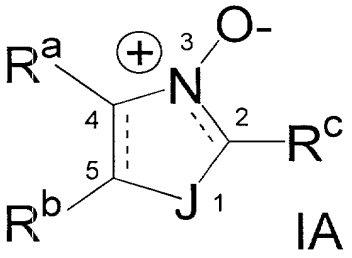

IA

wherein:

a. J is sulfur;

b. the carbon 2 to nitrogen bond is a double bond;

c. the bond between carbons 4 and 5 is a double bond;

d. R^a and R^b are independently selected from hydrogen, acylamino, alkanoyl, alkanoylalkyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C2-C6)hydroxyalkyl, nitro, trifluoromethyl, Ar {wherein, Ar is C_6 or C_{10} aryl}, or Ar–alkyl;

c. R^c is (C_2-C_5)alkyl omega-substituted with halo,

wherein aryl can be substituted with one or more substituents selected from the group of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C1-C3)alkylenedioxy, alkylthio, allyl, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C2-C6)hydroxyalkyl, mercapto, nitro, ArO-, Ar-, or Ar-alkyl-.